PATIENT REPORTED POSTOPERATIVE AND POSTDISCHARGE NAUSEA AND VOMITING FOLLOWING ORTHOGNATHIC SURGERY

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ABSTRACT

JESSE D. ARBON: Patient Reported Post-operative and Post-discharge Nausea and Vomiting following Orthognathic Surgery
(Under the direction of Dr. Ceib Phillips)

Postoperative nausea and vomiting (PONV) are common surgical sequelae. PONV coincides with physical morbidities and can increase recovery period, delay discharge, and lower patient satisfaction. The purpose of this study was to assess patients' experience with PONV following orthognathic surgery (OS). This prospective observational study enrolled 60 patients (ages 14-53) between 9/08 and 8/09 prior to OS. Patients completed a daily health diary each post-surgical day for 30 days. Data from medical/dental records were obtained to assess potential risk factors associated with patients' PONV experience. During the first 24 hours following OS, 58% of patients experienced significant nausea and 47% had an emetic event. 30% of subjects continued to report problems with PONV 5 days after being discharged. PONV has a high prevalence among orthognathic surgical patients. PONV continues to interfere with patient reported recovery nearly a week following surgery.

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SECTION I

LITERATURE REVIEW

No longer do health care practitioners practice in a paternalistic manner. Patients, now more than ever, are actively involved in health care decision making processes. Thus, it is the practitioner's responsibility to discuss in depth the risks and benefits associated with any treatment that may be rendered. For patients undergoing procedures that require anesthesia and surgery, it is equally important that they are well informed of both intra-operative and postoperative complications. In the United States alone, more than 71 million inpatient and outpatient operative procedures are performed each year. More than half (40 million) are reported as inpatient surgical procedures.[69] Although medical and pharmaceutical advancements have been achieved, postoperative nausea and vomiting (PONV) are some of the most frequent and distressing complications following inpatient and outpatient surgical procedures.[1] Accepted definitions of these factors are:

- Nausea: the involuntary sensation or impulse to vomit.
- Vomit: to expel the contents of ones stomach through the mouth.

Anatomy and Physiology

Although the physiology of the vomiting reflex is well understood, the pathways that control nausea and vomiting are not.[2] It is currently thought that the act of vomiting, or the impulse to do so, is controlled by a vomiting center. This center is located in the lateral reticular formation of the medulla oblongata in the midbrain stem central nervous system. It

is in close proximity to the fourth cerebral ventricle and to the nuclease of the vagus nerve (Figure 1). The area prostrema, which includes the chemoreceptor trigger zone (CTZ) is vascular but does not have an effective blood brain barrier. The area prostrema is laden with a variety of receptors including opioid, dopamine, histamine, cholinergic, 5-hydroxtryptamine (5-HT_3) and serotonin. Many anti-emetics target these receptors and antagonize their mechanism of action. Various pathways can stimulate and activate the vomiting center. The center receives afferent fibers from the periphery (GI tract, mediastinum, renal pelvis, peritoneum, genitalia) and from the central nervous system's cortical centers (visual center, vestibular apparatus, and CTZ zone) (Figure 2).[3-5] It has been and continues to be difficult to systematically and predictably study nausea and vomiting given the number of complex receptors and variety of intricate pathways that contribute to its occurrence.

Incidence

In 1984 Palazzo and Strunin[6] were some of the first to publish a comprehensive review of postoperative nausea and vomiting in the Canadian Anaesthetists' Society Journal. In 1992 Watcha and White[7] published a more universally recognized review on the etiology, treatment and prevention of PONV. Watcha and colleages comprehensively reviewed data from Palazzo's findings in conjunction with 150 relevant published articles since the 1984 Palazzo PONV review. Watcha found, in general, the approximate incidence of PONV following surgery varies between 20% and 30%. This is significantly lower than the 75-80% incidence reported during the "ether" era of general anesthesia.[7] This same incidence of 20-30% continues to be reported even in today's most recent peer reviewed literature.[8, 9] Watcha continued to report that there has been little change in the incidence of PONV since

the introduction of halothane in 1956 which widely replaced diethyl ether as a general anesthetic. Thus, Watcha's findings regarding the general incidence of PONV among the surgical population remains unchanged even today. In spite of significant medical and pharmaceutical advancements, little has been done to reduce the overall incidence of PONV over the past 54 years for surgical patients undergoing general anesthesia.

In addition to PONV's multifactorial nature, it is vitally important to recognize that the aforementioned level of incidence for PONV greatly depends on patient's individual, anesthetic and surgical risk factors.[6,10,11]

Risk Factors

Significant advances have been made in the past 20 years on identifying risk factors associated with PONV (Table 1). Although specific risk factors have been identified that are generally accepted and supported by sound evidence, mechanisms of PONV are still considered a multifactorial problem coupled with complex underlying biology.[12]

This review will primarily focus on risk factors that have been studied extensively and are widely accepted amongst the medical community as strong indicators for PONV. These include:

Patient Related

- Female gender[10,13- 20,23]
- History of motion sickness and/or PONV[10,13-17,19,20,23-25]
- Non-smoking status[10,13-19,27,28]
- Childhood after infancy and younger adulthood[25,32,33]

Surgical and Anesthesia Related

- Use of volatile anesthetics[15-17,34-36,39]

- Duration of anesthesia and/or surgery[10,13,15,24,25]
- Postoperative opioids[10,13,16,17,18,20,23,24,35,36,,40-43]

Probably the strongest risk factor identified is female gender. Most investigations report a significantly lower incidence of nausea and vomiting following surgery in males in comparison to females.[10,13- 20,23] Some of these studies have demonstrated that women tend to experience PONV two to three times more readily than men following surgical procedures. It's important to note that these gender differences are not observed in the prepubescent surgical population.[16,21] Thus, current theory believes the vomiting center is strongly influenced by the individual's endocrine and hormonal environment.[22]

Patients who report a history of PONV and/or motion sickness have also been identified as at risk patients for PONV.[10,13-17,19,20,23-25] It is thought that patients with a history of these factors have established a well developed reflex arc for vomiting.[16] Both a history of PONV and motion sickness are considered independent predictors for PONV. Although some researchers use and study these variables as separate predictors[13,23], combining the two into one predictive factor has been demonstrated to be a more dependable predictor for PONV.[10]

Nonsmoking status has been identified as an independent risk factor in a number of adult studies assessing PONV.[10,13-19,27,28] Odds ratios (OR) for adults with a nonsmoking status in these studies have been found to be approximately 1.5 to 2.5. Two theories exist as to why this phenomenon is observed. Some authors speculate that smoking may have an effect on the dopaminergic system thereby diminishing PONV.[29] The other and seemingly more plausible explanation is that chemicals inhaled through cigarette smoke effect the production of certain liver enzymes, especially cytochrome P450.[30] The increase in these

systemic liver enzymes result in the early metabolism of several ingested or inhaled drugs used during anesthesia, thus reducing the incidence of PONV.[31]

Generally speaking, increased age is associated with a decreased incidence of PONV. Within the pediatric population, postoperative emesis increases with age to reach a peak incidence in preadolescents around 11-14 year of age.[32] Prepubescent girls apparently lack the increased likelihood of PONV which implies that risk, as stated before, relates to certain hormonal factors.[25,33]

A number of anesthesia related variables have been well established as PONV risk factors. Especially the use of volatile inhalation anesthetics[15-17,34-36,39] (isoflurane, desflurane, sevoflurane, etc.) which when utilized, the incidence of PONV has been reported to occur twice as often when compared to the use of propofol anesthesia alone.[36] Due to their rapid metabolism, PONV associated with the use of volatile anesthetics usually occurs in the first two hours following surgery.[16] No significant difference in the risk of PONV has been found amongst the aforementioned volatile anesthetic agents.[33,36] Total IV anesthesia is a possibility and reports a lower incidence of PONV. However, it is usually restricted to shorter surgical procedures (less and 60min) due to the difficulty in maintaining normotensive or mildly hypotnesive mean arterial blood pressure.[37] Incorporation of a volatile inhalation agent, intravenous hypnotics and opioids is thought to be the best approach for rapid recovery with a lower incidence of PONV.[38,39]

The duration of surgery has also been shown to be an independent risk factor associated with PONV.[10,13,15,24,25] It has been reported that surgical duration lasting longer than 60 minutes increases a patient's risk of experiencing PONV. Sinclair et al[15] found that the prevalence of PONV increased from 2.8% in patients whose surgery was less than 30

minutes to 27.7% in patients with a surgical duration of 150-180 minutes. In summary this study indicated that every 30-minute increase in surgical time, resulted in a 60% increase in the baseline risk of PONV.[15]

It is well established that the use of intraoperative and perioperative opioids is strongly associated with PONV.[10,13,16,17,18,20,23,24,35,36,,40-43] Today, opioids are commonly used postoperatively for pain management. Opioids are thought to sensitize otic and vestibular areas to motion, resulting in PONV with movement.[7,44] Some researchers indicate that opiods are seldom the cause of PONV if patients are immobile.[45] Short acting opioids (ie, fentanyl, remifentanil, sulfentanil) are thought to cause less PONV in comparison to long acting opioids (ie, morphine, meperidine).[46] For example, morphine is associated with stimulation of the CTZ and vestibular apparatus, slowing of gastrointestinal motility, prolonged gastric emptying time and increased possibility of esophageal reflux which may induce emesis.[38,47]

Apfel at al[10] when analyzing four of the most widely accepted risk factors (female, hx of PONV/motionsickness, nonsmokers, postoperative opioids) found that the incidence of PONV was 10-21% in patients with no more than 1 risk factor. When two factors were present, the incidence rose to 39%. When three and four factors were identified for the same surgical patient, the incidence of PONV was reported to be 61% and 79% respectively. These findings have been further supported by two additional reports studying an inpatient surgical population.[12,55]

Type of Surgery

A number of studies have evaluated the incidence of PONV related to the type of surgery performed. Although there is some conflicting evidence, it is generally accepted that certain procedures carry an increased risk for PONV.[14-17,,35,41,48] These procedures include:

- Ear, nose and throat (ENT)[13,15,17-19,34,35,36,49]
- Gynecological[13,15-19,25,28,35,36]
- Opthalmologic[13,15,17-20,25,34,36,50,51,52,53]
- Neurosurgery[12,13,15,17,18,19,28,34,36,49,52]
- Laparoscopic[12,13,15,17,18,19,28,34,36,49,52,54]
- Intra-abdominal[12,13,15,17,18,19,28,34,36,49,52,54]

Among the above surgeries, the highest incidences of PONV have been reported at 80% for ophthalmaologic, 70% for ENT, 40-70% for intra-abdominal and 40-77% for laparoscopic surgeries. [13,15,17-20,25,34,36] Apfel et al.[10] found that type of surgery was not an independent risk factor for predicting PONV. When Apfel controlled for other risk factors, type of anesthetic and duration of operation, a causal effect on PONV by type of operation could not be established. These findings were all based on inpatient surgical cases. However in a large study of 18,000 ambulatory patients Sinclair et al[15] showed an increased risk for PONV (>15%) *among* patients undergoing dental surgery, orthopedic shoulder procedures, gynecologic laparoscopy, breast augmentation and strabismus repair.

The big little problem[55]

In 1991 Kapur described perioperative nausea and vomiting as "the big little problem" following ambulatory surgery.[55] Even though PONV is self-limiting and not fatal[56] it can result in significant morbidity. The undesirable sequela of PONV include dehydration,

electrolyte imbalance, suture tension and dehiscence, venous hypertension and bleeding, esophageal rupture, and life threatening airway compromise.[36,57]

Macario et al[58] utilized a preoperative survey and reported that patients ranked emesis as the most undesirable and nausea as the fourth most undesirable anticipated negative postoperative outcome. In this study gagging on the tracheal tube ranked second and pain ranked third. In another study examining patients' perception of PONV Gan et al[59] found that patients were, on average, willing to pay $56 out-of-pocket to avoid PONV; this dollar amount increased to $73 for patient who had experience postoperative nausea and to $100 in patients who had experienced postoperative vomiting. Studies have also suggested that not only do patients rank the absence of PONV as important but also rank it higher in importance than earlier discharge from outpatient surgical units.[58,60] PONV has also been shown to extend the recovery period, delay discharge, increase medical costs, and lower patient satisfaction scores.[7,62,63]PONV is clearly unsettling and creates considerable anxiety for both the recovering patient and his/her caregiver.

Post Discharge Nausea and Vomiting

Significant research associated with PONV it's risk factors and prevention has been performed in the last 20 years. It is important to note the majority of studies focus on the short-term incidence of PONV, meaning the first postoperative 24 hours. Furthermore, some patients experience PONV for the first time after discharge.[67] This distinguishment is important given the fact that as many as 35% - 50% of patients will experience post-discharge nausea and vomiting (PDNV).[63,64] However, very few studies have focused on and examined PDNV. Carroll et al[63] reported that patients with post-discharge nausea and vomiting require a longer time to resume normal daily activities. Carroll also reported that

nausea and vomiting in the immediate postoperative period may not accurately predict the incidence of nausea and vomiting after discharge from the hospital.[63] Wu et al[14] in 2002 published the first systematic review dedicated to post-discharge symptoms which included a thorough investigation of PDNV. This report indicated an incidence of 17% for nausea (range 0-55%) and 8% for vomiting (0-16%) after outpatient surgery. Philip et al[65] in a prospective multicenter survey reported even higher incidences of nausea and vomiting following ambulatory surgery. Nausea occurred in 46% of patients on postoperative day 1 and 8% on postoperative day 7. Vomiting occurred in 12% of patients on postoperative day 1 and 1% on postoperative day 7. Interestingly, nearly half the patients who did not have PONV in the hospital experienced nausea and/or vomiting on post-discharge days 1-3.[65] Gupta et al[66] examined published randomized, controlled trials to investigate whether routine antiemetic prophylaxis reduces the incidence of PDNV after ambulatory surgery in adults. Their comprehensive review reported a total of 815 patients who experienced post-discharge nausea(PDN) (32.6%). The number of patients who had PDN in the placebo and treatment groups were 276 (35.7%) and 539 (31.2%), respectively. Also reported in this review was a total of 497 patients who experienced post-discharge vomiting (PDV) (14.7%). In the placebo group, 19.6% of patients had PDV, whereas 12.1% of those in the treated group had PDV.[66]

Orthognathic Surgery

According to the American association of Oral and Maxillofacial Surgeons, "Corrective jaw, or orthognathic, surgery is performed by Oral and Maxillofacial Surgeons to correct a wide range of minor and major skeletal and dental irregularities, including the misalignment of jaws and teeth, which, in turn, can improve chewing, speaking and

breathing. While the patient's appearance may be dramatically enhanced as a result of their surgery, orthognathic surgery is performed to correct functional problems."

The first reported incidence of PONV in an orthognathic surgical population is reported in William R. Proffit's text book entitled "Contemporary Treatment of Dentofacial Deformity". In the final chapter on prevention and management of orthognathic surgical complications, page 695, Proffit reports that an unpublished review of 1000 consecutive orthognathic surgical cases was performed by Dr. Myron Tucker, a full time faculty member at the University of North Carolina School of Dentistry and UNC Hospitals from 1982 to 1992 where he was the director of graduate education in oral and maxillofacial surgery. Tucker found that 40% of his postoperative patients had at least one episode of nausea and/or vomiting. He further concluded that nausea due to swallowed blood was more common in two-jaw surgery because of increased hemmorage.[68]

Currently only one published study exists[9] that has reported the incidence of PONV in a sample of orthognathic sugery patients. Silva et al[9] conducted a retrospective cross-sectional survey of 553 consecutively treated patients over the age of 14. The patients underwent maxillary and/or mandibular osteotomies at Kaiser Permanente Hospital in Oakland, California between January 2003 to March 2004. Of the 514 patients that met the studies criteria, 40.08% experienced PONV during the first 24 hours after surgery. This retrospective analysis based the incidence of PONV on nursing notes made in the postanesthesia recovery room and the short-stay units while the patient was in the hospital. Silva et al[9] also analyzed risk factors that were associated with patients' that experienced PONV. They concluded that the most important predictive factors were female gender, young patients (15 to 25 years old), nonsmoking status, prior history of PONV/motion

sickness, use of volatile general anesthetics, maxillary surgery, postoperative pain level and the use of postoperative analgesic opioids. In addition they found a direct proportional relationship between the number of risk factors and the prevalence of PONV. Demonstrating that patient's reporting any 4 of the above risk factors was 58.8% more likely to experience PONV.[9]

In the current body of literature, there is no patient reported prospective documentation of PONV, let alone PDNV, following orthognathic surgery.

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SECTION II

MANUSCRIPT

INTRODUCTION

In the United States more than 71 million inpatient and outpatient surgical procedures are performed each year.[1] In the U.S. and in spite of significant medical and pharmaceutical advancements, post-operative nausea and vomiting (PONV) remain as frequent and distressing post-operative complications following inpatient and outpatient surgical procedures.[2]

Patients who have experienced PONV testify to its disturbing and unsettling nature. Patients have reported that PONV is a greater concern than that of post-operative pain.[3] In addition, patients who experienced PONV were willing to spend up to $100 dollars out of pocket for an effective antiemetic.[4] Studies suggest that not only do patients rank the absence of PONV as important but also rank it higher in importance than earlydischarge.[3,5] In addition to the acute episode of PONV, sequela include aspiration, deyhydration, electrolyte imbalances, gastric bleeding, hematoma, increased intracranial pressure, need to release intermaxillary fixation, pulmonary edema, and possible death.[6,7] PONV has also been shown to extend the recovery period, delay discharge, increase medical costs, and lower patient satisfaction.[6,8,9]

In general, it has been estimated that 20% to 30% of all patients experience PONV as a complication of surgery and anesthesia.[6,10,11,12] However the incidence greatly depends on

the patient's individual, anesthesia and surgical risk factors.[13,14,15] For instance, the frequency of PONV for patients with previously studied risk factors (female, history of motion sickness and/or PONV, nonsmoking status, use of post-operative opioids) in certain high risk procedures like ophthalmologic surgery, have been reported as high as 70-80%.[14,16,17] In addition, 30% to 50% of patients treated on an outpatient basis continue to experience post-discharge nausea and vomiting (PDNV).[9,18]

In a retrospective medical chart analysis, Silva et al.[19] reported 40% of patients who underwent orthognathic surgery experienced PONV during the first 24 hours following surgery. Estimates regarding the incidence of post-discharge nausea and vomiting (PDNV) are not currently available for orthognathic surgical patients. Understanding PONV and PDNV are particularly important when surgery is performed in an ambulatory care setting requiring patients to cope with post-operative sequela in the absence of direct medical supervision; resulting in considerable anxiety for both the recovering patient and his/her caregiver.[18] The purpose of this study was to prospectively assess the patient reported incidence, severity, duration, and risk factors associated with PONV and PDNV following orthognathic surgery.

MATERIALS AND METHODS

Sixty subjects, 14 years old and older, scheduled for an orthognathic surgical procedure for the correction of a dentofacial developmental disharmony or severe malocclusion between September 2008 and May 2009 at the University of North Carolina Memorial Hospital consented to participate in this prospective clinical study. Subjects were not excluded on the basis of sex or race. Subjects were excluded if they displayed one or more of the following attributes: congenital anomaly or history of acute facial trauma;

previous facial surgery; a medical condition associated with neuropathy (diabetes, hypertension, kidney problems); inability to follow written English instructions; unwilling to sign informed consent. The project was approved by the Biomedical Institutional Review Board.

A research associate described the project to each subject and obtained written consent or assent with parental permission and HIPPA authorization to review clinical records. All patients had undergone orthodontic preparation for orthognathic surgery and presented with fixed orthodontic appliances at the time of surgery. All orthognathic surgical procedures were performed by oral and maxillofacial surgery faculty and residents at N.C. Memorial Hospital. Semi- rigid fixation was utilized to stabilize bony jaw segments in conjuction with interocclusal wafers.

Accepted definitions in this study regarding PONV and PDNV are:

1. PONV: Post-operative nausea and vomiting while the patient was in the hospital (approximately 24 hours from surgical completion)
2. PDNV: Post-discharge nausea and vomiting starting from the time each patient was dismissed from the hospital.

Potential pre-, intra- and post-operative risk factors known to contribute to post-operative nausea and vomiting (PONV) were abstracted from each subject's medical chart. Preoperative data included demographic and health history variables; intra-operative data included surgical, anesthesia and pharmaceutical variables; post-operative data encompassed post-surgical medications and surgical/nursing notes to determine subjects' experience with PONV while in the hospital. Table 1 displays a more complete list of data gathered from medical charts.

A post-orthognathic surgical daily health diary (OSPostop) was modified to include specific items relating to nausea and emesis.[20,21] Subjects were asked to complete the diary each post-surgery day for 30 days. Nausea was rated on a 5 point scale from No Trouble/Concern (1) to Lots of Trouble/Concern (5). Subjects were also asked to report the presence/absence of emesis while in the hospital and each post-surgical day during the recovery period. Additionally, subjects were requested to record whether medications were taken for pain/discomfort and if so, what medications were taken and at what dose.

Subjects returned for routine post-operative visits with the surgical attending at one and four weeks. Subjects were asked to bring their completed diaries to these visits. If subjects failed to comply, a research associate provided the subject with pre-addressed and pre-metered envelopes to facilitate the diary return by mail.

Within the medical record: Inpatient progress notes, general progress notes, clinic note reports and discharge summary reports were evaluated to determine post-operative nausea. Reports for post-discharge nausea were stratified into two categories. Those scoring a 1 or 2 on the health diary each day were categorized as “No Substantial Interference”; while those scoring 3,4 or 5 were designated as having “Substantial Interference” with nausea. Additional data from medical charts were collected to evaluate potential risk factors associated with PONV (Table 2).

Data regarding post-operative and post-discharge vomiting were obtained from the OSPostop. Where patients reported presence/absence of emesis while in the hospital and each post-surgical day during the recovery period.

RESULTS

60 subjects consented to participate in this prospective observational study prior to orthognathic surgery. Seven subjects were dropped due to cancellation of their surgical procedure (insurance denied coverage, patient decided against surgery). Of the remaining 53 subjects, 39 (73%) completed and returned all 30 days of the recovery health diary. 1 patient had incomplete hospital records missing data required for this study (Figure 3).

Patients who participated were primarily female (68%) and Caucasion (63%). Subjects ranged in age from 15 to 48 years (median = 21 years; IQR = 17-27 years). Subjects were generally healthy and without systemic diseases (97% reported an ASA classification of 1 or 2). 37% had a procedure involving both jaws, 26% had a maxillary only procedure and 37% had a mandibular only procedure. See Table 3.

Medications

Evaluation of medical records (anesthesia, medication administration and post-anesthesia care records) revealed an extensive variety of administered medications. Peri- and intra-operatively greater than 90% of subjects received: benzodiazepines, local anesthetics, corticosteroids, short acting opioids (fentanyl), hypnotic, and antiemetics. All subjects received at least one or a two drug combination of volatile anesthetics and neuromuscular blocking agents. During the post-operative recovery period while in the hospital, greater than 90% were prescribed short acting opioids and antihistamines. Record analysis indicated a lack of specific protocols and inconsistencies in medical records regarding medications administered. The information available in the medical records was too vague and variable for statistical analysis.

PONV and PDNV

58% of subjects experienced nausea and 47% reported an emetic event while in the hospital (Figure 4). Forty-five percent of the subjects experienced nausea and 21% reported an emetic event after being released from the hospital (Figure 5).

29% of those who reported problems with post-discharge nausea did not have an emetic event while in the hospital. Three subjects (8%) reported experiencing nausea for the first time following discharge. Just over half (59%) of the subjects with post-discharge nausea reported no problems by day 3 after surgery. 5 patients (13%) reported problems with nausea up until the 5th postsurgical day (Figure 6).

Of the 18 patients who experienced emesis in the hospital, 8 (44%) had an additional emetic event following discharge. All patients who reported post-discharge vomiting had an emetic event and reported being nauseous in the hospital. Most (95%) patients reported complete resolution of vomiting by day 2 after surgery. Two patients reported emesis up until the 4th and 6th postsurgical day (Figure 6).

Relationship between Potential Risk Factors and PONV/PDNV

Simple cross-tabulations of potential risk factors and the occurrence of nausea and vomiting during the patients' hospital stay (PONV) are reported in Table 4 and post-discharge (PDNV) in Table 5. Patients' who indicated taking an opioid (oxycodone, hydrocodone or any medication with codeine) for pain management in their recovery diary on the first day following discharge were given a positive response for "patient reported opioid Rx".

Patient characteristics: In this sample males were more likely to experience PONV than females (Table 4). However, after discharge (Table 5) the proportion of males and females reporting PDNV was approximately the same. Teenage patients had an increased

likelihood compared to patients 20 years and older of PONV (Table 4) but not PDNV (Table 5). Subjects with a positive history of PONV and/or motion sickness were more likely to experience post-discharge nausea than post-discharge emesis. The previous history of PONV/motion sickenss did not appear to affect PONV.

Intra/post-operative characteristics: Patients undergoing a procedure involving maxillary surgery had an increased trend for both PONV and PDNV. Patients also had a strong likelihood of PONV with the administration of intra-operative nitrous oxide. Increased anesthesia time (≥ 180 minutes) appeared to increase the likelihood of patients experiencing post-operative nausea but not post-operative emesis or PDNV. The administration of post-operative long acting opioids (meperidine and/or morphine) appeared to be a strong indicator for patients experiencing PONV and post-discharge nausea. Likewise, patients who reported taking opioids after discharge seemed much more likely to experience PDNV.

DISCUSSION

Post-operative nausea and vomiting

Our study found a high incidence of PONV following orthognathic surgery. 58% of all subjects experienced nausea and 47% reported at least one emetic event while in the hospital. In 1992 Watcha et al[6] found the approximate incidence of PONV following surgery varies between 20% and 30%. This same level of incidence (20-30%) continues to be reported even in today's most recent peer reviewed literature.[10,19] Although there is some conflicting evidence, it is generally accepted that the risk for PONV is influenced by type of surgery. Ear, nose and throat (ENT), ophthalmologic, neurosurgery, gynecologic, laparoscopic and intra-abdominal surgeries have been identified as conduit procedures

increasing the risk for PONV.[22,25-30] Some of the highest incidences are reported at 80% for ophthalmaologic, 70% for ENT, 40-70% for intra-abdominal and 40-77% for laparoscopic surgeries.[7,12,26,28,31-35] Given the results of this study, orthognathic surgery should be regarded as a high risk procedure for PONV.

One published study has reported the incidence of PONV in a sample of orthognathic surgery patients. In a sample of 515 patients, Silva et al[19] found 40.1% experienced PONV during the first 24 hours after surgery. This level of incidence coincides with an unpublished review by Dr. Myron Tucker of 1000 consecutive orthognathic surgical cases at the University of North Carolina School of dentistry.[24] Differing levels of incidence in the aforementioned studies to our study may reflect dissimilarity in study design. Both Silva and Tucker performed retrospective analyses of patients' medical charts. In addition, both reviews combined nausea and vomiting as a single event as opposed to analyzing them separately. Our study prospectively analyzed patient reported experiences with both nausea and vomiting, but due to time requirements, cost, etc. associated with prospective longitudinal studies, our sample size was drastically smaller. Certainly more studies should be undertaken analyzing the relationship and differences between nausea and vomiting as two differing phenomena.

Post-discharge nausea and vomiting

Similar to PONV, we found a high incidence of PDNV was found with 44% of patients reported significant nausea and 21% reported at least one emetic event following discharge from the hospital. Gupta et al[36] examined PDNV after ambulatory surgery in adults and reported an incidence of 32.6% and 14.7% for post-discharge nausea and vomiting respectively. It is important to note the majority of studies analyze the short-term incidence

of PONV, meaning the first post-operative 24 hours. Furthermore, some patients experience PONV for the first time after discharge.[37] Few studies have focused on and examined PDNV, an important issue because even with the limited available data, as many as 35% - 50% of surgical patients will potentially experience PDNV.[9,18]

In our sample, 29% of those who reported problems with nausea after discharge did not have an emetic event while in the hospital, and 3 patients (8%) reported experiencing nausea for the first time following hospital discharge. Carrol et al.[9] reported that nausea and vomiting in the immediate post-operative period may not accurately predict the incidence of PDNV. Our data support this finding, although, in our sample, all patients who reported post-discharge vomiting had an emetic event and reported being nauseous in the hospital.

All subjects in our sample reached a full recovery within one week following surgery. Just over half (59%) of our subjects with post-discharge nausea reported no nausea and vomiting by day 3 after surgery. 5 (13%) patients reported problems with nausea up until the 5th postsurgical day. Most (95%) patients reported complete resolution of vomiting by day 2 after surgery. Two patients reported emesis up until the 4th and 6th postsurgical day. By the 7th postsurgical day all patients in our sample reported complete recovery from PDNV. Similarly, Philip and colleagues[38] also reported nausea occurred in 46% of patients on post-operative day 1 and 8% on post-operative day 7. Vomiting occurred in 12% of patients on post-operative day 1 and 1% on post-operative day 7.[38]

For patients undergoing procedures that require anesthesia and surgery, it is important that they are well informed of both intra-operative and post-operative complications. Since the 1980's, a gradual shift from inpatient surgical procedures to ambulatory surgery has occurred. This trend has continued even further and currently we see a shift in location from

an ambulatory setting to office-based surgical procedures involving anesthesia.[23] The Society of Ambulatory Surgery (SAMBA) currently reports 65% of all surgical procedures are now done on an outpatient basis.[23] Orthognathic surgery in many locations has mirrored such trends. As surgeons perfect techniques, technology continues to progress, health care costs continue to rise and patient and practitioner desires for convenience flourish; we suspect office-based orthognathic surgery will only increase in relation to inpatient surgery. Now more than ever, patients and practitioners need to understand the intricate aspects of surgical recovery; especially for patients who are required to cope with post-operative sequela, including PONV/PDNV, in the absence of direct medical supervision.

Potential risk factors

Potential risk factors evaluated in our study included: Female gender, age, history of PONV and/or motion sickness, type of surgery, use of intra-operative nitrous oxide, large intra-operative doses of neostigmine (≥ 2.5mg), post-operative long acting opioids and duration of anesthesia, all of which have been studied extensively and are widely accepted as strong indicators for PONV.[22] Although nonsmoking status and the use of volatile anesthetics are well established independent risk factors, these variables were not analyzed given that all 38 subjects received a volatile anesthetic during surgery and more than 90% reported they were non-smokers.

Due to the number of potential risk factors and sample size, we were not able to perform statistical analyses with sufficient power to demonstrate significance regarding risk factors and PONV/PDNV. Therefore descriptive statistics were performed and recorded in tables 3 and 4. Plausible trends in our sample for PONV were identified that are congruent with current evidence based literature.

PONV potential risk factors in our study supported by literature

Our teenage patients (< 20yrs old) demonstrated an increased likelihood of nausea, reporting an incidence of 65% compared to patients 20 years and older reporting a 52% incidence. Likewise, 53% of teenage patients reported an emetic event compared to 44% of patients 20 years and older. Increased age has been associated with a decreased incidence of PONV. Within the pediatric population, post-operative emesis increases with age to reach a peak incidence in preadolescents around 11-14 year of age.[39] Prepubescent girls apparently lack the increased likelihood of PONV which implies that risk may relate to certain hormonal factors.[34,40]

Maxillary only or 2 jaw procedures demonstrated a trend in the likelihood of PONV with 63% experiencing nausea compared to 50% who underwent mandibular surgery only. Emetic events in patients where the maxilla was involved reported a 54% incidence compared to 36% who did not. Silva et al[19] reported a statistically significant correlation with PONV when the maxilla was involved in the surgery.

Patients demonstrated increased nausea and vomiting when intra-operative nitrous oxide was used. 69% and 62% of patient administered nitrous oxide experienced nausea and vomiting respectively, compared to 31% who experienced nausea and 40% who reported emesis but were not prescribed intra-operative nitrous oxide. Administration of nitrous oxide is an established risk factor for PONV with incidence levels ranging from 49% - 67%.[35,40-44]

Patients who were administered post-operative long acting opioids (meperidine and/or morphine) appeared more likely to report nausea and vomiting recording an incidence of 62% and 52% respectively. While those who were not administered long acting opioids reported an incidence of 43% for nausea and 29% for emesis. It is well established that the

use of intra-operative and perioperative opioids is strongly associated with PONV.[12,14,21,22,27-29,31,33,44-47] Opioids are thought to sensitize otic and vestibular areas to motion, resulting in PONV with movement.[6,48] Short acting opioids (ie, fentanyl, remifentanil, sulfentanil) are thought to cause less PONV in comparison to long acting opioids (eg, morphine, meperidine).[49] Morphine is associated with stimulation of the chemoreceptor trigger zone (CTZ) and vestibular apparatus which may induce emesis.[50,51]

Increased anesthesia time (≥ 180 minutes) appeared to increase the percent of patients experiencing PONV. 65% of patients with a total anesthesia time greater than 180 minutes experienced nausea while 50% with less than 180 total anesthesia time reported nausea. The duration of surgery has also been shown to be an independent risk factor associated with PONV.[14,26,31,34,44] It has been reported that surgical duration lasting longer than 60 minutes increases a patient's risk of experiencing PONV. Sinclair et al[26] found that the prevalence of PONV increased from 2.8% in patients whose surgery was less than 30 minutes to 27.7% in patients with a surgical duration of 150-180 minutes. Stated slightly differently, Sinclair indicated that every 30-minute increase in surgical time, resulted in a 60% increase in the baseline risk of PONV.[26]

PONV trends unique to this study

Our study did not demonstrate that female gender was a strong indicator for PONV when in fact it is probably the strongest risk factor identified in the literature. Most investigations report a significantly lower incidence of nausea and vomiting following surgery in males in comparison to females.[12,14,25-28,31-33,52] Some studies have quantified that women tend to experience PONV two to three times more readily than men following surgical procedures. It's important to note that these gender differences are not observed in

the prepubescent surgical population.[27,53] Thus, current theory believes the vomiting center is strongly influenced by the individual's endocrine and hormonal environment.[54] The risk with small sample sizes is that the sample may not be a true representation of the desired surgical population. However, given that this is the first prospective observation of PONV/PDNV for orthognathic surgical patients, the high incidence of PONV for males should not be discounted and commands further investigation.

Likewise, for subjects with a positive history of PONV and/or motion sickness, our sample did not demonstrate increase PONV. History of PONV and/or motion sickness has also been identified placing a patient at risk for PONV. [14,31,25-28,32,33,34,44,52] It is thought that patients with a history of these factors have established a well developed reflex arc for vomiting.[27] Both a history of PONV and motion sickness are considered independent predictors for PONV. However combining the two into one predictive factor has been demonstrated to be a more dependable predictor.[14] In this study, these data were gathered from medical charts. Retrospectively gathering data on such forms assumes with certainty that physicians asked the appropriate health history questions and recorded them correctly. It is possible that this data was incomplete and did not reflect the samples absolute response to inquiries related to health history.

Potential post-discharge nausea and vomiting risk factors

With a limited number of studies evaluating PDNV; strong prospective indicators for PDNV have not been well established. It has been advocated by some that PDNV carries similar risk factors to PONV including: female gender, young age, history of PONV and/or PONV in the PACU, and perioperative opioids.[23] Data from our study does coincide with some of the aforementioned suggested risk factors. In our sample patients reporting a history

of PONVand/or motion sickness portraid and increase in the likelihood of post-discharge nausea. 83% of those with a positive history for PONV and/or motion sickness reported experiencing nausea after discharge. 48% of patients who received long acting opioids also reported post-discharge nausea compared to 29% who did not receive long acting opioids. Patients who took opioids after discharge seemed much more likely to experience post-discharge nausea and vomiting reporting incidences of 58% and 25% respectively. Minimal data is available for PDNV. The high incidence in our study and others warrants more studies with a primary focus on PDNV to determine its incidence, duration, relationship to PONV and potential risk factors.

Although our understanding of risk factors associated with PONV his increased dramatically over the past 30 years, reduction of its occurrence has not significantly improved. The incidence for post-operative nausea and vomiting in orthognathic surgical patients is high. PONV and PDNV continues to plaque orthognathic surgical patient recovery up to a week following hospital discharge. Now more than ever, patients and practitioners need to understand the intricate aspects of surgical recovery; especially for patients who are required to cope with post-operative sequela, including PONV/PDNV, in the absence of direct medical supervision.

CONCLUSIONS

- The incidence of PONV in orthognathic surgical patients remains high.
- The incidence of PDNV appears to be greater than 20%
- The occurrence of PONV/PDNV can cause discomfort up to a week following orthognathic surgery.

- Surgical procedures involving a maxillary osteotomy appear to increase the likelihood of PONV and PDNV.
- Patients who were administered long-acting and post-operative opioids appear more likely to experience PONV and PDNV.

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Figure 1. Anatomical relationships of the brain involved with nausea and vomiting[www.nauseaandvomiting.co.uk]

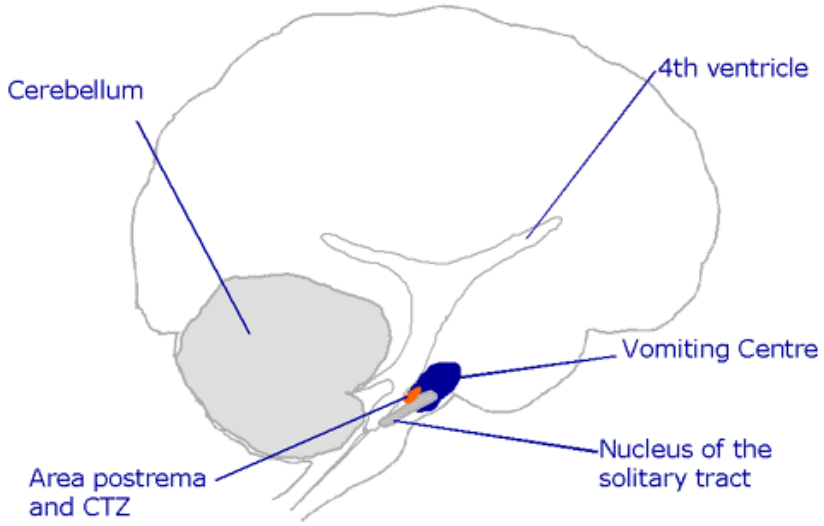


Figure 2. Mechanisms and neurotransmitter pathways of PONV[Silva et al, 2006]

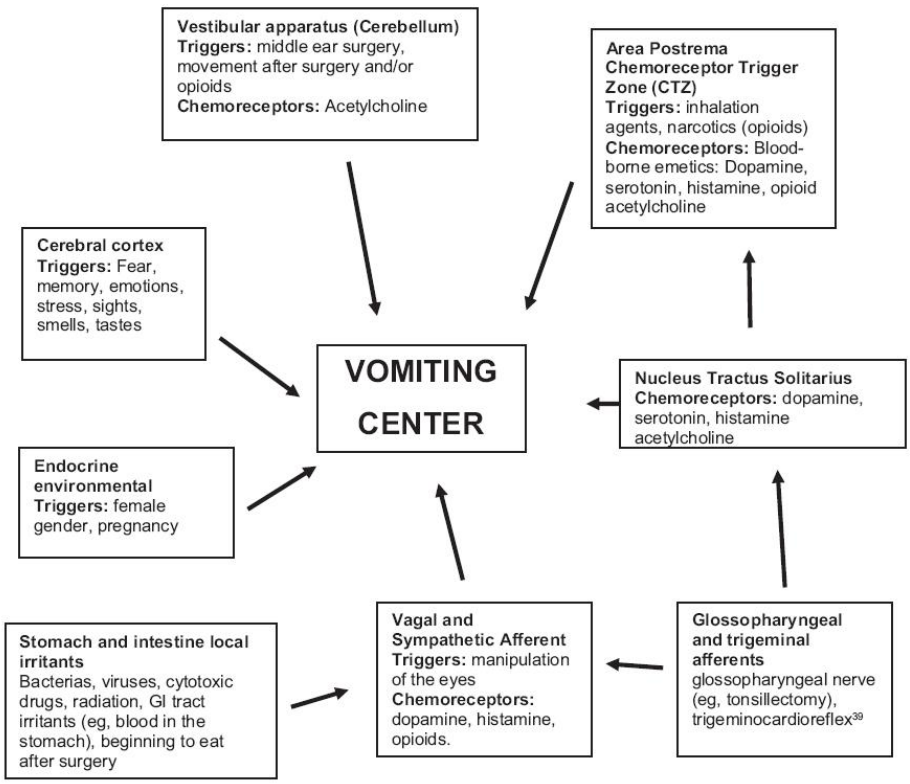


Table 1. Risk factors for postoperative nausea and vomiting Apfel et al. 2003

Positive results with strong clinical impact	Mostly positive results	Conflicting results	Flawed or insufficient data	Disproved factors
Female gender	Young age and physical status	Site of surgery	Pain	Body mass index
History of motion sickness or PONV	Nitrous oxide	Menstrual cycle	Movement	
General versus regional anesthesia	Muscle relaxant antagonists	Experience of the anaesthetist	Anxiety and personality	
Volatile anesthetics		Gastric tube for decompression of the stomach		
Non-smoking status				
Duration of anaesthesia				
Postoperative opioids				

PONV: Postoperative nausea and vomiting.

Table 2. Potential preoperative, intraoperative and postoperative risk factors for PONV

Preoperative Characteristics	Intraoperative Characteristics	Postoperative Characteristics
Age **Gender** **Race** Caucasian vs. Non-Caucasian **Body Mass Index** Underweight (BMI <18.5) Normal weight (BMI <18.5-24.9) Overweight (25-29.9) Obese (30 or greater) **Mallampati Score** I, II, II or IV **American Society of Anesthesia Status** I, II, II or IV **History of PONV** **History of Motion Sickness** **History of GERD**	**Type of Surgery** Mandibular only Maxillary only Bimaxillary (2J) **Additional Procedures** Extraction of 2 or more 3rd molars Genioplasty **Anesthesia duration** **Surgical duration (incision to dressing)** **Intraoperative medications** ex: opioids, neuromuscular blockers (NMB), NMB reversal agents, antiemetics, hypnotic, nitrous oxide, volatile anesthetics, etc. **Blood loss**	**Post-op meds administered in hospital** ex: long acting opioids(morpine & meperidine), antiemetics, etc. **Surgeon/Nursing notes** Relating to PONV

Figure 3. Subject Selection Flow Chart

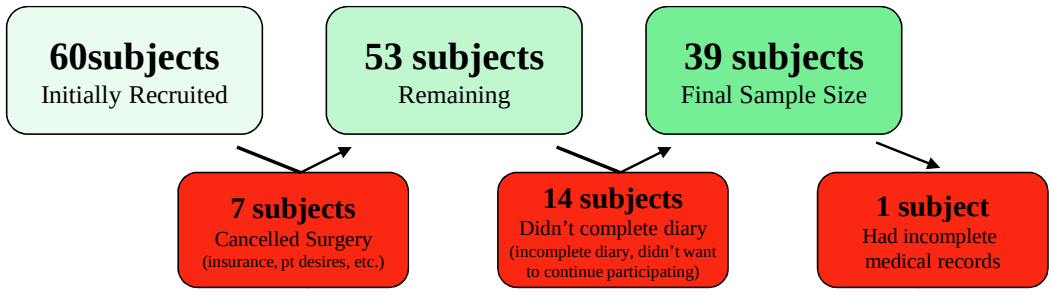


Table 3. Demographic and Surgical Characteristics

	N	%
Female	26	68
Male	12	32
Caucasian	24	63
Other	14	37
Age		
Teenager (14-19)	17	45
Twenties	13	34
Thirties	5	13
Forty and over (40-48)	3	8
Type of Sx		
Two Jaw	14	37
Maxilla only	10	26
Mandible only	14	37

Figure 4. Patient Reported PONV while in the Hospital

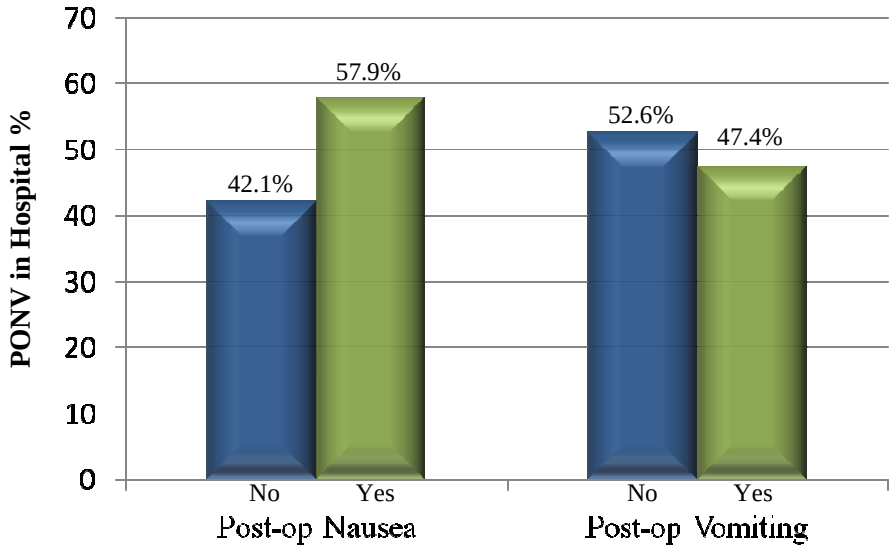


Figure 4. Patient Reported Post Discharge Nausea and Vomiting

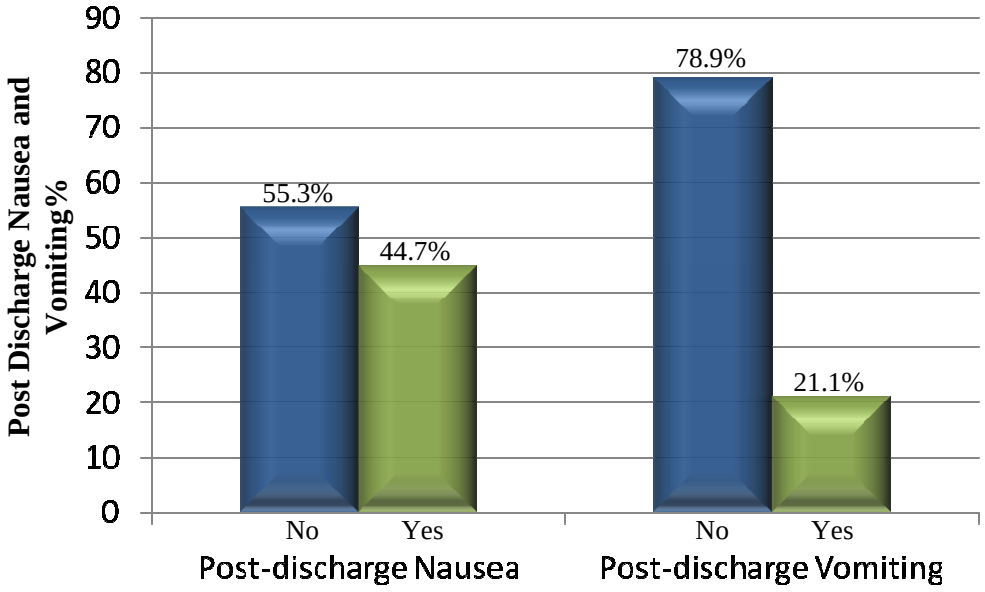
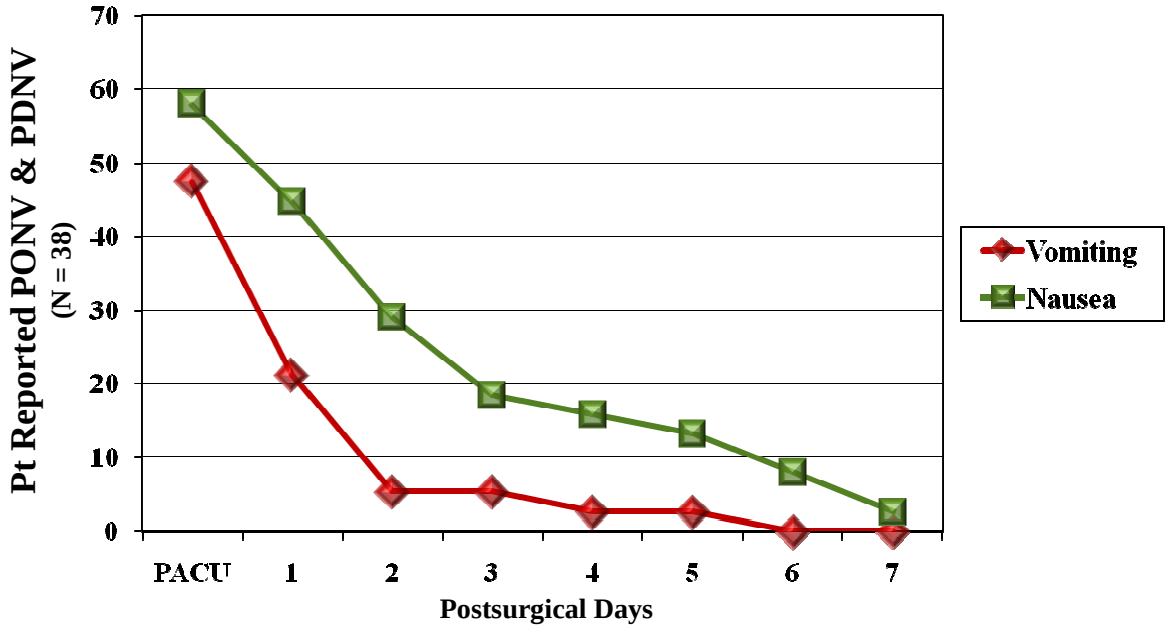


Figure 6. Patient reported PONV & PDNV following orthognathic surgery



(PACU=Post Anesthesia Care Unit)

Table 4. Potential Risk Factors and PONV while in Hospital

Potential Risk Factors		Nausea		Vomiting	
		No	Yes	No	Yes
Gender					
	Female	46.1%	53.9%	61.5%	38.5%
	Male	33.3%	66.7%	33.3%	66.7%
Age					
	< 20 yrs old	35.4%	64.7%	47.1%	52.9%
	≥ 21 yrs old	47.6%	52.4%	57.1%	42.9%
Hx of PONV/ Mot. Sickness					
	No	41.9%	58.1%	54.8%	45.2%
	Yes	50.0%	50.0%	50.0%	50.0%
Type of Surgery					
	Mand only	50.0%	50.0%	64.3%	35.7%
	Mx or 2 jaw	37.5%	62.5%	45.8%	54.2%
Intra-op Nitrous Oxide					
	No	48.0%	30.8%	60.0%	40.0%
	Yes	52.0%	69.2%	38.5%	61.5%
Intra-op neostigmine					
	< 2.5	34.6%	65.4%	50.0%	50.0%
	≥ 2.5	58.3%	41.7%	58.3%	41.7%
Post-op long acting opioids					
	No	57.1%	42.9%	71.4%	28.6%
	Yes	38.7%	62.3%	48.4%	51.6%
Duration of anesthesia					
	< 180 min	50.0%	50.0%	55.6%	44.4%
	≥ 181 min	35.0%	65.0%	50.0%	50.0%

Table 5. Potential Risk Factors and PDNV

Potential Risk Factors		PD Nausea		PD Vomiting	
		No	**Yes**	**No**	**Yes**
Gender					
	Female	54%	46%	81%	19%
	Male	58%	42%	75%	25%
Age					
	< 20 yrs old	59%	41%	76%	24%
	≥ 21 yrs old	52%	48%	81%	19%
Hx of PONV/ Mot. Sickness					
	No	61%	39%	81%	19%
	Yes	17%	83%	83%	17%
Type of Surgery					
	Mand only	64%	36%	93%	7%
	Mx or 2 jaw	50%	50%	71%	29%
Duration of anesthesia					
	< 180 min	50%	50%	83%	17%
	≥ 181 min	60%	40%	75%	25%
Post-op long acting opioids					
	No	71%	29%	86%	14%
	Yes	52%	48%	77%	23%
Pt reported opioid Rx					
	No	80%	20%	100%	0%
	Yes	42%	58%	75%	25%